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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/003,983	10/31/2001	Hans Josef Stauss	ICI 103	6029

23579 7590 09/21/2006

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EXAMINER	
DIBRINO, MARIANNE NMN	
ART UNIT	**PAPER NUMBER**
1644	

DATE MAILED: 09/21/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/003,983	STAUSS ET AL.	
	Examiner	Art Unit	
	DiBrino Marianne	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *11 July 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *2-6 and 8-42* is/are pending in the application.

4a) Of the above claim(s) *5 and 8-41* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *2-4, 6, 42* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 7/11/06 has been entered.

Applicant's amendment filed 7/11/06 is acknowledged and has been entered.

2. Applicant is reminded of Applicant's election with traverse of Group I (claims 2-4, 6 and 42), and species of SEQ ID NO: 1 containing peptide bonds in Applicant's response filed 2/2/05.

Claims 2-4, 6 and 42 read on the elected species, SEQ ID NO: 1, and are presently being examined.

3. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

4. Claims 2-4, 6 and 42 are rejected under 35 U.S.C. 103(a) as being unpatentable over WO 97/26328 A1 (IDS reference) in view of The Leukocyte Antigen Fact Book (2nd edition, pages 244-247, 1997, IDS reference), Rammensee *et al* (MHC Ligands and Peptide Motifs, LANDES Bioscience, Springer, NY, 1997, pages 217-227 and 236-281, of record), WO 99/45954 A1, US 7,063,854 B1 and Sievers (Curr. Opin. Immunol. 12: 30-35,1/00).

WO 97/26328 A1 teaches a method of treating a disease, including leukemia, comprising administering allo-restricted allogeneic CTL specific for peptides from self proteins, for example from WT1, that are expressed in tumors and in a limited number of normal cells, tissue-specific differentiation antigens, and in the case of leukemia CTL with specificity for leukemias can be generated against peptides that are expressed in leukemic cells but not in cells outside the hematopoietic lineage and then used for adoptive immunotherapy of leukemia patients where they will eliminate leukemic cells and possibly some normal bone marrow derived cells. WO 97/26328 A1 teaches that possible loss of normal bone marrow cells is not expected to cause any problems because these patients are frequently treated with bone marrow transplantation from healthy donors (see entire article, especially page 19 at lines 21-30 and continuing onto page 20 at lines 1-5 and page 23 at lines 11-19). WO 97/26328 A1 further teaches that

known CTL epitope peptides or newly identified peptides may be used, in the latter instance, the peptides that bind to a particular HLA class I molecule may be identified and may represent better targets for adoptive immunotherapy since they are likely to be subdominant peptides that are less likely to be immunoselected by the patient's CTL responses. WO 97/26328 A1 teaches methods for generating said CTL, and that the stimulator cell has a type of HLA class I molecule that is not present on the healthy individual's cells, and further teaches testing of binding to HLA class I molecules and for generating and stimulating CTL. WO 97/26328 A1 teaches that HLA-A0201 is particularly preferred allele that is present on the stimulator cells at a high frequency in the human population (page 27 at lines 19-30 and page 28 at line 1).

WO 97/26328 A1 does not teach the CD45 peptides recited in the instant claims 2-4, 6 and 42 that consist of or comprise SEQ ID NO: 1.

The Leukocyte Antigen Fact Book teaches that CD45 protein(s) are found on all cells of hematopoietic origin, except erythrocytes, and further teaches the amino acid sequence of the human CD45 protein and that it is 1281 amino acid residues in length.

Rammensee *et al* teach anchor residue motifs for peptides that bind to individual class I MHC molecules (HLA in humans) including HLA-A*0201, and that most peptides that bind class I molecules are between 8 and 11 amino acid residues in length consonant with the length of peptide required to span the class I MHC binding groove. Rammensee *et al* teach methods of predicting MHC class I peptide epitopes using motifs to identify subsequences possessing the motif in proteins of interest. Rammensee *et al* teach that the motif for peptides that bind to HLA-A*0201 is L or M at position 2 of the peptide and V or L at the carboxy-terminal position of the peptide, but that other endogenous peptides as well as CTL epitope peptides that bind to HLA-A*0201 may have I, T, M or A at position 2 as well, and A, I, T, S or C at the carboxy-terminus. Rammensee *et al* teach that most peptides that bind to HLA-A*0201 are 9 to 10 amino acid residues in length (pages 271-227 and 236-281).

WO 99/45954 A1 teaches methods for selecting immunogenic peptides capable of specifically binding HLA molecules and inducing T cell activation (abstract). WO 99/45954 A1 teaches identifying peptides from target proteins that are capable of binding to an HLA molecule by using the binding motif for a particular class I HLA molecule to search for peptides having the motif. WO 99/45954 A1 teaches testing the peptides for binding to said HLA molecule and teaches methods for said testing. WO 99/45954 A1 further teaches assaying the binding peptides for their ability to induce specific CTL responses *in vitro*, and methods for said assaying, and testing the CTL for their ability to lyse target cells. WO 99/45954 A1 teaches that HLA-A2.1 (*i.e.*, HLA-A*0201) is expressed at high frequency in Caucasoid and Asian populations (pages 7-8, page 10 at lines 13-32, page 11, page 12 at lines 1-12).

US 7,063,854 B1 discloses immunogenic compositions comprising MHC class I binding peptides from WT1 tumor antigen protein that stimulate CTL, and that may further comprise MHC class II binding peptides that stimulate Th (*i.e.,* Th provide help for antibody production and for CTLp). US 7,063,854 B1 discloses that the pharmaceutical compositions may comprise WT1 peptides that can elicit both CD4+ and CD8+ (*i.e.,* Th and CTL) responses. US 7,063,854 B1 further discloses that a CD45 peptide antigen is capable of stimulating T cells, as well as disclosing prediction of HLA-A*0201 binding peptides from CD45 that are potentially capable of binding and eliciting CTL and prediction of T cell epitope peptides that potentially function as Th epitopes. US 7,063,854 B1 discloses peptides that tested positive for binding to HLA-A*0201 and were capable of eliciting a CTL response (especially abstract, column 28 at lines 53-64, column 29, column 30 at Table III, column 61, claims, column 18 at lines 27-67, column 19, column 20 at lines 1-61).

Sievers teaches that CD45 is a target antigen for the majority of leukemia cells as well as for normal stem cells, and an antibody specific for CD45 is useful in combination with conventional preparative regimens for patients receiving marrow transplantation for acute leukemia, as well as for targeting radiation *in vivo* (especially abstract, last paragraph of article, page 33 at column 2 and page 34 through the first full paragraph at column 1).

It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to have used the method of epitope prediction taught by Rammensee *et al* and WO 99/45954 A1 using the peptide binding motif of a frequently expressed HLA molecule such as HLA-A*0201 to scan the human CD45 protein sequence taught by The Leukocyte Antigen Fact Book and by Sievers for subsequences that would potentially bind to HLA-A0201 and function to stimulate CTL as taught by Rammensee *et al* and by WO 97/26328 A1, in effect to generate peptides of 9 amino acid residues in length that would be predicted to bind to HLA-A*0201 from the sequence of human CD45 protein, said peptides having the motif anchor residues at positions 2 and 9 or 10, and to have produced the peptides recited in the instant claims comprising or consisting of SEQ ID NO: 1 which is a subsequences of human CD45 that has the anchor residues taught by Rammensee *et al*, and to have tested synthetic peptide versions of them as per the teaching of WO 99/45954 A1 for binding to HLA-A*0201 and for their ability to stimulate CTL, and as per the teaching of WO 97/26328 A1 for identifying peptides that bind to a particular HLA class I molecule from differentiation antigens such as WT-1 expressed in leukemic cells or from proteins expressed in leukemic cells but not in cells outside the hematopoietic lineage.

It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to have made the said peptides and tested them for potential use in the method taught by WO 97/26328 A1 for generating allo-restricted CTL for use in adoptive immunotherapy of leukemia patients.

One of ordinary skill in the art at the time the invention was made would have been motivated to do this in order to generate peptides as per the teaching of Rammensee *et al* and WO 99/45954 A1 using the human CD45 protein sequence taught by The Leukocyte Antigen Fact Book that are candidate peptides for binding HLA-A*0201 and for stimulating CTL as taught by WO 99/45954 A1 for potential use in the method taught by WO 97/26328 A1 of identifying peptides that can bind to alleles present in high frequency in the population such as HLA-A0201 for generation of allo-restricted CTL that are useful in treating leukemia patients. One of ordinary skill in the art at the time the invention was made would have been motivated to do this because WO 97/26328 A1 teaches that allo-restricted CTL that are specific for peptides that are expressed on leukemic cells but not in cells outside the hematopoietic lineage are useful to treat patients with leukemia and that such a use is not expected to cause any problems due to possible loss of normal bone marrow cells because these patients are frequently treated with bone marrow transplantation from healthy donors and further teaches using WT1 peptides, The Leukocyte Antigen Fact Book teaches that the human CD45 protein is found on all cells of hematopoietic origin, Sievers teaches that CD45 is a target antigen for the majority of leukemia cells as well as for normal stem cells and the usefulness of targeting CD45 to treat leukemia; and US 7,063,854 B1 discloses that CD45 peptide is capable of eliciting a CTL response and pharmaceutical compositions comprising peptides from another leukemia antigen WT1 that bind to class I or class II MHC to treat leukemia.

Applicant's arguments have been fully considered, but are not persuasive.

Applicant's arguments are of record in Applicant's said amendment on pages 9-14 under the section entitled "Rejection Under 35 U.S.C. 103." It is Applicant's position that: (1) none of the references alone or in combination disclose or suggest a peptide of 9-12 amino acid residues in length, wherein the peptide contains the sequence of SEQ ID NO: 1, or a position 2 and/or position 9 variant thereof, (2) none of the references provide the motivation to combine said references, (3) the WO document does not disclose CD45 as being a target for tumor immunotherapy, (4) the instant specification discloses on page 2 at lines 18-19 that CD45 is expressed in hematopoietic malignancies at similar levels as expressed on normal cells and the WO document discloses that the antigen for the CTL is expressed abnormally, so there would not exist motivation to combine the references, (5) the references do not provide a reasonable expectation of success, (6) predictive methods do not always predict actual binding affinity so there is no way of knowing based on the Rammensee reference whether any CD45 peptides generated through their method would bind an HLA molecule, (7) Applicant inserted the CD45 sequence into a web-based algorithm based on Rammensee to search for 10-mer peptides that bind to HLA-0201 which generated a list of hundreds of peptides without guidance for which would bind, (8) Rammensee does not provide a reasonable expectation of success for peptides with binding affinity that are also immunogenic, but Applicant experimentally generated immunogenic peptides from CD45, (9) Fikes discloses epitopes of an antigen that is not CD45, and so does not

provide a reasonable expectation of success for which peptides of CD45 bind and are immunogenic.

It is the Examiner's position that: (1) the references are being argued separately, (2) that the motivation to combine references is provided by the teaching of the WO 97/26328 A1 document that CTL with specificity for leukemias can be generated against peptides that are expressed in leukemic cells, but not in cells outside the hematopoietic lineage, such peptides deriving from "self proteins that are expressed in tumors and in a limited number of normal cells (tissue-specific differentiation antigens)", "tissue-specific proteins that are expressed in tumors", "CTL with specificity for leukaemias can be generated against peptides which are expressed in leukaemic cells but not in cells outside the haematopoietic lineage", and target proteins such as "WT-1" and "GATA-1," combined with the teaching of the Human Leukocyte Handbook that CD45 is a protein with expression limited to cells of hematopoietic lineage except for erythrocytes, Sievers teaches that CD45 is a target antigen for the majority of leukemic cells as well as for normal stem cells, and US ,063,854 B1 discloses that a CD45 peptide could generate a CTL response, (3) and (4) the WO 97/26328 A1 document discloses suitable target proteins for treatment of leukemia such as WT-1 and GATA-1 (that are disclose in Applicant's specification on pages 1-2 to be suitable targets for CTL against leukemia, said proteins being expressed on normal cells), and although the WO 97/26328 A1 document discloses classes of target proteins such as those expressed abnormally on tumor cells, it also discloses using differentiation antigens of the hematopoietic lineage that are also expressed on leukemic cells, and the Human Leukocyte Handbook discloses that CD45 is such a differentiation antigen, so the motivation to combine references exists, (5) and (6) the instant claims are not drawn to a method of predicting peptides that bind to an HLA molecule and elicit a CTL response, but rather to a product that is capable of binding to HLA-A0201 and eliciting a CTL response; the combined references provide motivation to make a nonamer peptide that is a subsequence of CD45 protein with L2/T9 anchor residues with the expectation that it might bind to HLA-A2 and stimulate a CTL response and WO 99/45954 A1 and Rammensee et al teach a method for predicting such peptides, testing binding and the ability to stimulate CTL, (7) the claimed peptide is a 9-mer not a 10-mer peptide, the portion of Rammensee *et al* that was cited by the Examiner teaches using primary anchor residues to predict HLA binding peptides, although non-cited portions of the book do contain teaching of using computer based algorithms incorporating use of secondary anchor residues and knowledge of deleterious residues at other positions, such as the web-based algorithm used by Applicant, and the web-based algorithm does provide a ranking of those peptides most likely to bind; however, these are side-issues. The teaching of using primary anchor residues to predict binding peptides in combination with the other cited references provides motivation to make the FLYDVIAST peptide because it might bind to HLA-A2 since it has anchor residues, and it is not required that the references provide a teaching for predicting which peptides are immunogenic since the instant claims are not drawn to a method for predicting binding peptides and immunogenicity, and (8) Fikes is not cited in the instant rejection. In

response to Applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986). The recited properties of binding to HLA-A0201 and being capable of eliciting CTL are expected properties of the art peptide.

5. Claims 2-4, 6 and 42 are rejected under 35 U.S.C. 103(a) as being unpatentable over WO 97/26328 A1 (IDS reference) in view of The Leukocyte Antigen Fact Book (2nd edition, pages 244-247, 1997, IDS reference), LANDES Bioscience, Springer, NY, 1997, pages 217-227 and 236-281, of record), U.S. Patent No. 6,602,510 B1 (of record), U.S. Patent No. 7,063,854 B1 and Sievers (Curr. Opin. Immunol. 12: 30-35, 1/00).

WO 97/26328 A1 teaches a method of treating a disease, including leukemia, comprising administering allo-restricted allogeneic CTL specific for peptides from self proteins, for example WT1, that are expressed in tumors and in a limited number of normal cells, tissue-specific differentiation antigens, and in the case of leukemia, CTL with specificity for leukemias can be generated against peptides that are expressed in leukemic cells but not in cells outside the hematopoietic lineage and then used for adoptive immunotherapy of leukemia patients where they will eliminate leukemic cells and possibly some normal bone marrow derived cells. WO 97/26328 A1 teaches that possible loss of normal bone marrow cells is not expected to cause any problems because these patients are frequently treated with bone marrow transplantation from healthy donors (see entire article, especially page 19 at lines 21-30 and continuing onto page 20 at lines 1-5 and page 23 at lines 11-19). WO 97/26328 A1 further teaches that known CTL epitope peptides or newly identified peptides may be used, in the latter instance, the peptides that bind to a particular HLA class I molecule may be identified and may represent better targets for adoptive immunotherapy since they are likely to be subdominant peptides that are less likely to be immunoselected by the patient's CTL responses. WO 97/26328 A1 teaches methods for generating said CTL, and that the stimulator cell has a type of HLA class I molecule that is not present on the healthy individual's cells, and further teaches testing of binding to HLA class I molecules and for generating and stimulating CTL. WO 97/26328 A1 teaches that HLA-A0201 is particularly preferred allele that is present on the stimulator cells at a high frequency in the human population (page 27 at lines 19-30 and page 28 at line 1).

WO 97/26328 A1 does not teach the CD45 peptides recited in the instant claims 2-4, 6 and 42.

The Leukocyte Antigen Fact Book teaches that CD45 protein(s) are found on all cells of hematopoietic origin, except erythrocytes, and further teaches the amino acid sequence of the human CD45 protein and that it is 1281 amino acid residues in length.

U.S. Patent No. 6,602,510 B1 discloses that peptides that bind to HLA class I molecules are about 8 to about 13 amino acid residues in length and possess amino acid residues at certain positions in the peptide sequence that are required for allele-specific binding. U.S. Patent No. 6,602,510 B1 discloses that a supertype motif is a peptide binding specificity shared by HLA molecules encoded by two or more HLA alleles, and that vaccines which bind to HLA supertypes such as A2, A3 and B7 will afford broad, non-ethnically biased population coverage. U.S. Patent No. 6,602,510 B1 discloses that the HLA-A2 supermotif is L, I, V, M, A, T or Q at position 2 of the peptide, and I, V, M, A, T or L at the carboxy-terminus of the peptide. U.S. Patent No. 6,602,510 B1 discloses that 9-mer subsequences of tumor-associated antigenic proteins were scanned to identify potential HLA-A2 supertype allele binding peptides, *i.e.,* that would bind to HLA-A0201 as well as other alleles in the supertype (especially column 18 at lines 34, column 2 at lines 58-column 3 at lines 1-3, column 13 at lines 11-15, Table 2 and 2A, Table 4).

US 7,063,854 B1 discloses immunogenic compositions comprising MHC class I binding peptides from WT1 tumor antigen protein that stimulate CTL, and that may further comprise MHC class II binding peptides that stimulate Th (*i.e.,* Th provide help for antibody production and for CTLp). US 7,063,854 B1 discloses that the pharmaceutical compositions may comprise WT1 peptides that can elicit both CD4+ and CD8+ (*i.e.,* Th and CTL) responses. US 7,063,854 B1 further discloses that a CD45 peptide antigen is capable of stimulating T cells, as well as disclosing prediction of HLA-A*0201 binding peptides from CD45 that are potentially capable of binding and eliciting CTL and prediction of T cell epitope peptides that potentially function as Th epitopes.
US 7,063,854 B1 discloses peptides that tested positive for binding to HLA-A*0201 and were capable of eliciting a CTL response (especially abstract, column 28 at lines 53-64, column 29, column 30 at Table III, column 61, claims, column 18 at lines 27-67, column 19, column 20 at lines 1-61).

Sievers teaches that CD45 is a target antigen for the majority of leukemia cells as well as for normal stem cells, and an antibody specific for CD45 is useful in combination with conventional preparative regimens for patients receiving marrow transplantation for acute leukemia, as well as for targeting radiation *in vivo* (especially abstract, last paragraph of article, page 33 at column 2 and page 34 through the first full paragraph at column 1).

It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to have used the method of epitope prediction disclosed by U.S. Patent No. 6,602,510 B1 using the peptide binding motif of a frequently expressed HLA molecule such as HLA-A*0201 to scan the sequence of the human CD45 leukemia tumor/differentiation antigen taught by Sievers to be a target for treatment of leukemia having the sequence taught by The Leukocyte Antigen Fact Book, in a manner similar to that disclosed by US 7,063,854 B1 for the WT1 leukemia antigen to identify subsequences that would potentially bind to HLA-A*0201 and function to stimulate CTL

as disclosed by U.S. Patent No. 6,602,510 B1 and as taught by WO 97/26328 A1, in effect to generate peptides of 9 or 10 amino acid residues in length that would be predicted to bind to HLA-A*0201 from the sequence of human CD45 protein, said peptides having the motif anchor residues at positions 2 and 9 or 10, and to have produced the peptides recited in the instant claims comprising or consisting of SEQ ID NO: 1 which is a subsequences of human CD45 that has the anchor residues disclosed by U.S. Patent No. 6,602,510 B1.

It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to have identified peptides of appropriate length and motif potentially capable of binding to an HLA-A*0201 class I MHC molecule as per the disclosure of U.S. Patent No. 6,602,510 B1 from the CD45 human protein taught by Siever with the protein sequence taught by The Leukocyte Antigen Fact Book and to have tested synthetic peptide versions of them as per the teaching of WO 97/26328 A1 and as per the disclosure of U.S. Patent No. 6,602,510 B1 and US 7,063,854 B1 for their ability to bind to HLA-A*0201 and stimulate a CTL response for potential use in the method taught by WO 97/26328 A1 for generating allo-restricted CTL with specificity for peptides that are expressed in leukemic cells but not in cells outside the hematopoietic lineage, said allo-restricted CTL useful for adoptive immunotherapy of leukemia patients.

One of ordinary skill in the art at the time the invention was made would have been motivated to do this because WO 97/26328 A1 teaches that allo-restricted CTL that are specific for peptides that are expressed on leukemic cells but not in cells outside the hematopoietic lineage are useful to treat patients with leukemia and that such a use is not expected to cause any problems due to possible loss of normal bone marrow cells because these patients are frequently treated with bone marrow transplantation from healthy donors, The Leukocyte Antigen Fact Book teaches that the human CD45 protein is found on all cells of hematopoietic origin and Sievers teaches that CD45 is a target antigen for the majority of leukemia cells as well as for normal stem cells. One of ordinary skill in the art at the time the invention was made would have been motivated to do this because WO 97/26328 A1 teaches that allo-restricted CTL that are specific for peptides that are expressed on leukemic cells but not in cells outside the hematopoietic lineage are useful to treat patients with leukemia and that such a use is not expected to cause any problems due to possible loss of normal bone marrow cells because these patients are frequently treated with bone marrow transplantation from healthy donors, and The Leukocyte Antigen Fact Book teaches that the human CD45 protein is found on all cells of hematopoietic origin.

One of ordinary skill in the art at the time the invention was made would have been motivated to do this because WO 97/26328 A1 teaches the method using peptides from target antigens such as WT1 and the usefulness of the method in treating leukemia, Sievers teaches that CD45 is a target antigen for the majority of leukemia cells as well as for normal stem cells and the usefulness of targeting CD45 to treat leukemia, US 7,063,854 B1 discloses that CD45 peptide is capable of eliciting a CTL response and using peptides from anther leukemia antigen WT1 that bind to class I or class II MHC in the same pharmaceutical composition to treat leukemia. One of ordinary skill in the art at the time the invention was made would have been motivated to do this in order to generate peptides as per the disclosure of U.S. Patent No. 6,602,510 B1 using the human CD45 protein sequence taught by The Leukocyte Antigen Fact Book to use in the method taught by WO 97/26328 A1 of identifying peptides that can bind to alleles present in high frequency in the population such as HLA-A0201 for generation of allo-restricted CTL that are useful in treating leukemia patients.

Applicant's arguments have been fully considered, but are not persuasive.

Applicant's arguments are of record in Applicant's said amendment on pages 9-14 under the section entitled "Rejection Under 35 U.S.C. 103."

Applicant's arguments have been fully considered, but are not persuasive.

The Examiner's position enunciated supra at item #4 of this Office Action apply herein, except that Fikes *et al* is being argued separately. The recited properties of binding to HLA-A*0201 and being capable of eliciting CTL are expected properties of the art peptide.

6. No claim is allowed.

7. Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Marianne DiBrino whose telephone number is 571-272-0842. The Examiner can normally be reached on Monday, Tuesday, Thursday and Friday.

If attempts to reach the examiner by telephone are unsuccessful, the Examiner's supervisor, Christina Y. Chan, can be reached on 571-272-0841. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Marianne DiBrino, Ph.D.
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September 8, 2006

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